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E D I T O R I A L

On these pages the editor offers his opinions, unshackled by advertising patrons and unrestrained by anything save a sense of the decent and the truthful – the editor, alone, is responsible for their type, their tone and their tenor.

CHROMATOTHERAPOLOGY!!

COLOR is one of those difficultly definable terms. The schoolboy avers that there is no color in the dead of night, the physicist insists that color, like the note in music, is an undulating expression of energy, with color related to light as pitch is to sound. And the artist, wiser than all the rest, mixes his colors with intuition, and spreads them on canvas, or elsewhere, to be a soothing inspiration to generations yet unborn.

Everyone knows the story of Sir Isaac Newton, who, intense in his study of natural phenomena, was impelled to the discovery of the law of Gravitation, when a tree-tired apple let go its hold and emphatically fell on his head.

But few persons know that Newton also discovered the law of color. For it was he who first described the octave-like spectrum, that division of light into its eye-visible fractions, violet, indigo, blue, green, yellow, orange and red. Under the violet and over the red, we now know that in the realm of invisible light there are ranges of wave lengths, too short or too long for the human eye to record. Incidentally, the spectrum had been man's privilege to see, ever since the Lord of Israel had hung on high his inverted and discarded bow without the arrow (the rainbow), a token to arrant sons of earth that never again would mundane sins be penalized with water. So much for the general aspects of color.

A rose, when red, is red because it keeps or absorbs the other spectral hues, and only gives the brain-informing eye its red vibrations. Obviously then, since color—a form of energy—really reaches the brain, it must have mental influence.

Chromatotherapology is the science dealing with the effect of color on the human body. Strangely enough, interior decorators have regarded this study with much more practical respect than have physicians. For instance, although rarely done, it would be perfectly *reasonable* for a doctor to prescribe a lavender color scheme, and lav-

ender wall paper, draperies, clothes, and even lavender medicine, for a highly neurotic patient; and especially so if the patient was obese, or a natural blond. Such a prescription would be thoroughly scientific.

Red excites, and so to a lesser degree do orange and yellow. Shades of violet, indigo and blue have a calming effect, although the livid blue, the cyanotic blue, is melancholic. Generally green gives pleasure, and then a sense of peace, yet there are yellow greens that nauseate.

Red, in some of its hues and values, constricts large spaces, red-painted rooms appearing both confiningly hot and tight, but red emphasizes the size of smaller objects. Thus a pink-colored pill appears larger than a like-sized pill coated with the light-absorbing chocolate. Lighter blues belie the borders of a room, and with their hints of summer heavens, bring calm to tired souls. Certain yellows are bilious, unfriendly, especially in the chrome range. Yet they are said to stimulate the flow of bile, and so assist intestinal digestion. Does red, by the same token, incite the spleen and marrow to haematopoietic riot?

We have practical demonstrations of mind's sway over matter, of the psychic over the physic, with respect to our other senses. So why not with color?

The sound of trickling water is a psychic diuretic, and "music hath its charms to soothe the savage breast."

The touch of a loving hand dispels despair, and the blended scents of flowers excite the brain to lovely memories. A roast in the oven conveys its noseward message from kitchen to street, and spurs the gastric juice of hungry passers-by to idle stimulation.

And as the sense of taste has therapeutic implications, so we must assume that color, too, tinctures the physiologic picture.

IVOR GRIFFITH.

ORIGINAL ARTICLES

NOTES CONCERNING RELATIVE TOXICITY OF THE THREE HALIDES OF LITHIUM UPON GREEN MOLD (PENICILLIUM ITALICUM)*

By Bernard Melkon[1] M. Sc.

THIS problem was studied with the hope of adding to an ever-enlarging body of scientific data concerning the effects of the action of chemical elements and compounds upon the growth of numerous fungus foes.

Fungi cause enormous losses to fruits, vegetables and other foodstuffs, and some of the pharmaceutical and biological products also may not escape from the infection of these plants, if these products are not properly protected.

The green mold (Penicillium italicum) produces a rot of citrus fruits, and subsequently causes a great financial loss in all important orange growing countries.

The main factor of infection has been shown to be the wounding of fruits.

The prevention of wounding has been advocated by all workers, but the treatment of fruits with chemicals has also been used to inhibit the infection of oranges by green mold (Penicillium).

Three lithium halides have been selected for investigation of their relative toxic action upon the growth of Penicillium italicum.

Method and Procedure—The parent culture of the fungus, Penicillium italicum, was obtained from the U. S. Department of Agriculture, Washington, D. C. A colony was obtained from a single spore of this culture, by inoculation of 10 cc. culture solution, described below, containing 3 per cent. agar.

Culture Solution—The composition of the culture solution employed was as follows:

Orange, dry weight	50 g. per liter
Cane Sugar	20 g. per liter
$Ca(NO_3)_2$ 0.5 M.	4 cc. per liter
$MgSO_4$ 0.5 M.	2 cc. per liter
K_2HPO_4 0.5 M.	4 cc.
Distilled water	1000 cc.

*Philadelphia Meeting, Plant Science Seminar, 1937.

[1] Biology Department, Philadelphia College of Pharmacy and Science.

The juice of the oranges was obtained by squeezing it, by means of a fruit press; then to this juice enough distilled water was added to make 1000 cc.; then the other ingredients were added and mixed thoroughly.

The final pH of the medium was adjusted by the addition of sufficient N/1 NaOH to bring the pH to 5.2.

The same size of platinum loop was always used for inoculation.

Two methods of inoculation were used during these experiments. (1) In the first method a loopful of spores was taken from the inoculation tube, containing the fungus growing on 3 per cent. agar in standard nutrient solution, and added to each flask containing nutrient solution. (2) In the second method the shape of platinum wire was modified (but the loop remained unchanged) and used as follows:

The platinum wire was bent twice at 90 degrees. The first bend was made approximately ½ inch from the loop; the second bend being at the junction of the wire with the loop, so that the loop became parallel with the glass handle (See Fig. 1).

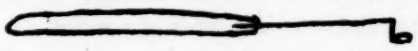

Fig. 1

The loop only was moistened by immersing it in the nutrient medium to be inoculated, then the surface of the fungus, growing on 3 per cent. agar in standard nutrient solution, was gently touched with this moist loop, which thus became charged with the spores. This loop, now carrying spores, was immediately immersed again in the same flask containing the nutrient medium from which the moist loop was first withdrawn.

The advantage of the second method is that only the moist platinum loop touches the fungus spores, and assures almost a uniform quantity of inoculum.

After the inoculation by either method, the flasks were rotated in order to distribute the spores in culture medium.

Chemicals—The lithium salts were obtained from Merck and Co., Inc.

Experimental data—The normal solutions of LiI, LiBr, LiCl were used in the experiment.

Series consisting of four Erlenmeyer flasks, each flask containing 50 cc. of nutrient solution and a determined volume in cc., of the salt

solution to be used (see tables) were inoculated, in a ventilated inoculation chamber, with spores from 11 days old orange-juice slant. After 21 days of incubation the contents of each flask were then filtered through a filter paper, which was previously heated at 90° C. in an electric oven for 48 hours in order to determine its constant weight at that temperature.

The residue was washed with distilled water for several times.

The properly-numbered filter papers, with fungus, were then dried in an electric oven at 90° C. for 48 hours. They were then cooled in a desiccator and weighed separately.

The weight of fungus on each filter paper was obtained by subtracting the weight of the filter paper from the weight of the filter paper and the fungus.

The results of the effects of the various salts are shown in three tables. Reading from left to right, the first column of each table shows the series, the number of which depends upon the number of cc. of solution used.

The second column shows the number of cc. of the solution tested for toxicity, added to each flask of a series.

Columns 3-14 are divided into four groups, each of which presents the results of the experiment of each flask in each series; thus column 3 shows the weights of dried filter paper and fungus, column 4 shows the weights of dried filter paper, and column 5 shows the weight of dried fungus of flask No. 1. The quantitative data yielded by flasks 2, 3 and 4 are shown in columns 6, 7, 8, 9, 10, 11, 12, 13, and 14 respectively.

Column 15 indicates the average weight of the dried fungus of each series.

Column 16 indicates the percentage weight of the dried fungus of each series, based upon the average weight of dried fungus grown in control flasks.

The average weight of the dried fungus obtained from the series of control flasks in each experiment, has been considered 100 per cent. for that particular experiment, shown in each table. Percentage growth has been calculated for each experiment on the basis of 100 per cent. growth for control flasks.

A critical study of the tables will reveal some variations in the results of the experiments. These variations may probably be attributed to some of the following causes:

(a) Range of room temperature
(b) Difference in temperature (2-3° C.) between the upper and lower shelves of incubator
(c) The viscous state of the liquid contents of some flasks, rendered filtration very difficult.
(d) Methods of inoculation.

Discussion

A study of the tables shows that, although each flask of each series was treated under the same conditions and contained the same substances, the weight of fungus of each flask varies from the others. In order to minimize the errors of final results, four flasks of each series were used.

A comparison of the toxicity of equinormal solutions of the three halogen salts of lithium (Fig. 2) shows that they are toxic to the growth of Penicillium italicum in the following order: LiI, LiBr, LiCl.

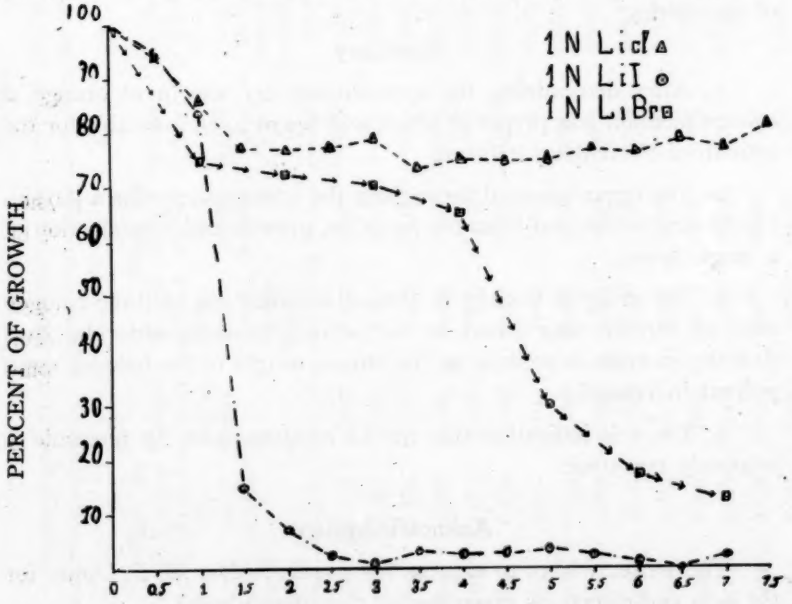

Fig. 2—Percentage of growth of Penicillium italicum at normal solutions of three halogen salts of lithium.

The order of toxicity of these salts suggests that as the atomic weight of the halogen component increases, its toxicity also increases.

If the lithium were the part of the molecule of these salts which had a toxic effect upon Penicillium italicum, apparently the salts should not show such great range of variation of toxicity.

The characteristic criteria of high toxicity of any one of these salts upon Pencillium italicum were taken to be pronounced wrinkling of the mycelial mat on the surface of the nutrient medium, scattered patches of mycelium or absence of growth.

The weight of the dried fungus, obtained from control flasks for an experiment, has been considered to be 100 per cent. for that experiment carried out at that particular time.

The best method of inoculation may be considered to be the one, by the use of which, a uniform amount of inoculum may be added to each flask. This may be proven by the comparison of the weights of dried fungus (columns 5, 8, 11 and 14) obtained from each flask of each series.

Summary

1. After determining the approximate dry weight of orange, a culture medium was prepared which was found to be favorable for the growth of Penicillium italicum.

2. The organism used throughout the investigation was a physiological strain obtained from the isolation, growth and reproduction of a single spore.

3. The order of toxicity to Penicillium italicum, of three halogen salts of lithium was found to be iodide>bromide>chloride, thus showing increase in toxicity as the atomic weight of the halogen component increased.

4. There is indication that the Li component of the molecule is relatively non-toxic.

Acknowledgment

The writer wishes to express his thanks to Dr. M. S. Dunn, for the help and directions given during this investigation.

TABLE I

EXPERIMENTAL DATA SHOWING THE INFLUENCE OF LITHIUM IODIDE UPON PENICILLIUM ITALICUM

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
		Flask #1			Flask #2			Flask #3			Flask #4				
Series of flasks	Cc. of normal solution of Lithium Iodide in each flask	Weight of dried filter paper and fungus in gms.	Weight of dried filter paper in gms.	Weight of dried fungus in gms.	Weight of dried filter paper and fungus in gms.	Weight of dried filter paper in gms.	Weight of dried fungus in gms.	Weight of dried filter paper and fungus in gms.	Weight of dried filter paper in gms.	Weight of dried fungus in gms.	Weight of dried filter paper and fungus in gms.	Weight of dried filter paper in gms.	Weight of dried fungus in gms.	Average weight of dried fungus in gms.	% growth based on normal growth
I	½	1.580	1.053	0.527	1.593	1.057	0.536	1.542	1.004	0.538	1.621	1.098	0.523	0.531	95.160
II	1	1.521	1.038	0.483	1.512	1.045	0.467	1.490	1.029	0.461	1.504	1.042	0.462	0.468	83.870
III	1½	1.249	0.982	0.267	1.032	1.017	0.015	1.049	1.017	0.032	1.103	1.080	0.023	0.084	15.053
IV	2	0.952	0.928	0.024	1.084	0.970	0.114	1.025	1.006	0.019	1.031	1.020	0.011	0.042	7.526
V	2½	1.109	1.063	0.046	1.155	1.149	0.006	0.866	0.866	0.000	0.944	0.934	0.010	0.015	2.688
VI	3	0.895	0.890	0.005	0.917	0.904	0.013	0.995	0.989	0.006	0.879	0.876	0.003	0.007	1.250
VII	3½	0.933	0.906	0.027	1.025	1.003	0.022	0.976	0.971	0.005	0.998	0.970	0.028	0.020	3.584
VIII	4	0.952	0.944	0.008	0.904	0.878	0.026	0.960	0.949	0.011	0.850	0.837	0.013	0.014	2.508
IX	4½	0.960	0.850	0.024	0.843	0.830	0.013	0.977	0.964	0.013	0.916	0.902	0.014	0.016	2.867
X	5	0.967	0.940	0.027	0.906	0.888	0.018	0.898	0.872	0.026	0.848	0.831	0.017	0.022	3.942
XI	5½	0.790	0.779	0.011	0.934	0.928	0.006	1.045	1.026	0.019	0.926	0.915	0.011	0.012	2.150
XII	6	0.942	0.940	0.002	0.874	0.867	0.007	0.879	0.865	0.014	0.828	0.828	0.000	0.006	1.075
XIII	6½	0.902	0.902	0.000	0.909	0.909	0.000	0.899	0.899	0.000	0.890	0.890	0.000	0.000	0.000
XIV	7	0.957	0.934	0.023	0.967	0.965	0.002							0.012	2.150
XV	Control	1.533	0.964	0.569	1.467	0.904	0.563	1.520	0.971	0.549	1.510	0.951	0.559	0.558	100

TABLE II

EXPERIMENTAL DATA SHOWING THE INFLUENCE OF LITHIUM BROMIDE UPON PENICILLIUM ITALICUM

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
			Flask #1			Flask #2			Flask #3			Flask #4				
Series of flasks	Cc. of normal solution of Lithium Bromide in each flask	Weight of dried filter paper and fungus in gms.	Weight of dried filter paper in gms.	Weight of dried fungus in gms.	Weight of dried filter paper and fungus in gms.	Weight of dried filter paper in gms.	Weight of dried fungus in gms.	Weight of dried filter paper and fungus in gms.	Weight of dried filter paper in gms.	Weight of dried fungus in gms.	Weight of dried filter paper and fungus in gms.	Weight of dried filter paper in gms.	Weight of dried fungus in gms.	Average weight of dried fungus in gms.	% growth based on normal growth
I	1	1.559	1.1795	0.3795	1.540	1.157	0.383	1.589	1.1945	0.3945	1.5735	1.1745	0.399	0.388	74.95
II	2	1.558	1.174	0.384	1.452	1.0675	0.3845	1.517	1.160	0.357	1.524	1.1425	0.3815	0.377	72.63
III	3	1.4735	1.110	0.3635	1.508	1.159	0.349	1.503	1.145	0.358	1.493	1.0945	0.3985	0.365	70.32
IV	4	1.438	1.0885	0.3495	1.548	1.205	0.343	1.541	1.170	0.371	1.521	1.224	0.297	0.340	65.51
V	5	1.490	1.225	0.265	1.248	1.165	0.083	1.1785	1.0945	0.084	1.334	1.1635	0.1705	0.150	29.9
VI	6	1.269	1.0945	0.1745	1.2235	1.183	0.0405	1.239	1.160	0.079	1.248	1.180	0.068	0.090	17.34
VII	7	1.113	1.039	0.074	1.1845	1.099	0.0855	1.1645	1.119	0.0455	1.1835	1.123	0.0605	0.066	12.71
VIII	Control	1.367	0.853	0.514	1.553	1.008	0.545	1.418	0.912	0.506	1.457	0.937	0.520	0.519	100

TABLE III

EXPERIMENTAL DATA SHOWING THE INFLUENCE OF LITHIUM CHLORIDE UPON PENICILLIUM ITALICUM

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
			Flask #1			Flask #2			Flask #3			Flask #4			
Series of flasks	Cc. of normal solution of Lithium Chloride in each flask	Weight of dried filter paper and fungus in gms.	Weight of dried filter paper in gms.	Weight of dried fungus in gms.	Weight of dried filter paper and fungus in gms.	Weight of dried filter paper in gms.	Weight of dried fungus in gms.	Weight of dried filter paper and fungus in gms.	Weight of dried filter paper in gms.	Weight of dried fungus in gms.	Weight of dried filter paper and fungus in gms.	Weight of dried filter paper in gms.	Weight of dried fungus in gms.	Average weight of dried fungus in gms.	% growth based on normal growth
I	½	1.299	0.8295	0.4695	1.412	0.904	0.508	1.389	0.932	0.457	1.4085	0.912	0.4965	0.483	94.33
II	1	1.415	0.962	0.453	1.376	0.942	0.434	1.432	1.003	0.429	1.498	1.072	0.426	0.435	85.95
III	1½	1.2885	0.910	0.3785	1.277	0.863	0.414	1.406	1.009	0.397	1.350	0.955	0.395	0.396	77.33
IV	2	1.245	0.8445	0.4005	1.302	0.9215	0.3805	1.279	0.881	0.398	1.369	0.976	0.393	0.393	76.75
V	2½	1.426	1.015	0.401	1.350	0.944	0.406	1.279	0.893	0.386	1.505	1.101	0.404	0.399	77.93
VI	3	1.472	1.0625	0.4095	1.2985	0.908	0.3905	1.373	0.965	0.408	1.286	0.878	0.408	0.404	78.90
VII	3½	1.394	1.018	0.376	1.3945	1.0115	0.383	1.387	1.010	0.377	1.3495	0.982	0.3675	0.376	73.43
VIII	4	1.279	0.881	0.398	1.4545	1.076	0.3785	1.315	0.932	0.383	1.408	1.0335	0.3745	0.383	74.80
IX	4½	1.462	1.0825	0.3795	1.445	1.076	0.369	1.385	1.003	0.382	1.385	0.9925	0.3925	0.381	74.40
X	5	1.274	0.890	0.384	1.3225	0.933	0.3895	1.395	1.013	0.382	1.454	1.068	0.386	0.385	75.2
XI	5½	1.292	0.887	0.405	1.399	0.9935	0.4055	1.391	0.9895	0.4015	1.424	1.0545	0.3695	0.395	77.14
XII	6	1.433	1.054	0.379	1.414	1.010	0.404	1.388	1.001	0.387	1.365	0.982	0.383	0.390	76.16
XIII	6½	1.462	1.051	0.411	1.370	0.9685	0.4015	1.4385	1.035	0.4035	1.390	0.988	0.402	0.404	78.90
XIV	7	1.3835	0.970	0.4135	1.3685	0.9690	0.3995	1.3915	0.9965	0.3950	1.3645	0.965	0.3995	0.401	78.32
XV	7½	1.3815	0.939	0.4425	1.343	0.9245	0.4185	1.4045	1.0035	0.4010	1.3765	0.9635	0.4130	0.419	81.83
	Control	1.485	0.952	0.533	1.521	1.018	0.503	1.534	1.0225	0.5115	1.600	1.101	0.499	0.512	100

COMPARATIVE STUDIES ON THE PHYSICAL PROPERTIES OF THE CALCIUM SALT OF VITAMIN C, CALCIUM CEVITAMATE, AS COMPARED TO CALCIUM GLUCONATE.

By Dr. Simon Ruskin, New York

SOLUBLE salts of Calcium that may be used therapeutically possess importance in view of the extremely limited number of available preparations. In fact, Calcium Gluconate or the glucono gluconate represents the only source of calcium for intramuscular use.

In view of the close chemical relationship between gluconate and cevitamates, both being sugars, the cevitamate differing in the possession of a double bond and two nitrogen atoms less, it was surprising to observe a unique difference in solubilities in the calcium salts of the gulconate and the cevitamate. Whereas the calcium gluconate is soluble only to the degree of 3 per cent., the Calcium Cevitamate is practically 100 per cent. soluble, in fact it may be considered hygroscopic.

In view of the marked solubility of Calcium Cevitamate a difference in ionization of the two salts suggested itself and the following experiments were performed and the results recorded.

Salt	% Solution by Weight	Concentration Moles/Liter	Temp. Drop °C.	% Ionization	Yield Ca. ion per gram Salt	Yield Ca. ion per cc. Solution
Calcium Cevitamate	5%	.123	.577	74.6	.0700	.0037
Calcium Cevitamate	10%	.261	1.085	60.0	.0563	.0063
Calcium Cevitamate	20%	.589	2.362	58.1	.0545	.0137
Calcium Cevitamate	30%	1.008	3.940	55.3	.0528	.0226
Neo-Gluconate	10%	.125	.565	*47.8	.0323	.0048
Neo-Gluconate	20%	.273	1.120	*40.3	.0273	.0088
Calglucon	3%	.072	.263	48.6	.0452	.0014

An analysis of these findings would tend to indicate that the Calcium Cevitamate in 5 per cent. solution was approximately equivalent to the neo-gluconate in 10 per cent. solution and that the 10

*Since the structure of the Neo-Calgluconate is not known, and since its empirical formula is $(C_{36}H_{64}O_{38})Ca_2$, we have assumed that it ionizes as follows: $Ca_2C_{36}H_{64}O_{38} \rightarrow 2\,Ca + 2(C_{18}H_{32}O_{19})$.

per cent. Calcium Cevitamate was approximately equivalent to the 20 per cent. neo-gluconate.

The comparative series was run only to 30 per cent. Calcium Cevitamate because the neo-gluconate solutions do not exceed 20 per cent. In considering the calglucon tablet which is only 3 per cent. soluble the yield of calcium ions per cc. of solution was .0014 whereas that of the Calcium Cevitamate in only 30 per cent. solution was .0226 or about twenty times greater. If calculated on the basis of 100 per cent. it would be in the vicinity of sixty times greater in calcium ion content per cc. solution. How important this factor can be in the question of calcium absorbability becomes apparent from the volume of solute necessary to obtain an equal amount of available calcium. For every 100 cc. of solute required for the absorption of Calcium Cevitamate it would require 6000 cc. of solute for an equal availability of calcium in calcium gluconate. Since the total fluid content of the gastro-intestinal canal is about 5000 cc. and absorption of calcium occurs only in the upper intestine, the difference in absorbability between Calcium Cevitamate and calcium gluconate becomes apparent.

The action of cevitamic acid on the ionization of calcium opens up a field both of theory and practice. A comparison of the physiologic action of cevitamic acid and calcium shows an almost completely parallel action in bone metabolism, hemorrhagic diathesis, cell membrane permeability and detoxicating action. So close is this resemblance that one can interchange their functions. It is this element which suggests that cevitamic acid may be the factor which acts as the vehicle for the diffusible fraction of the serum calcium. There is a strong probability that the parathyroid hormone and cevitamic acid jointly balance the small fraction of ionized diffusible calcium. Greenwald is quoted by Cantarow as suggesting that some of the calcium is bound to an organic substance in a citrate like combination, the compound being intimately connected with the parathyroid hormone probably diffusible and slightly ionized. Belief in the existence of such a compound is also shared by Klinke and by Dendroy and Hastings. The latter drew attention to the similarity of action of the parathyroid hormone and citrate solutions in holding calcium in solution. In view of the fact that calcium citrate is only .8 per cent. soluble it is difficult to conceive of citrate as a calcium solubilizing agent. Cevitamic acid, however, has precisely the desired action

on the ionization of calcium and its distribution in the intestinal canal, pituitary and adrenal makes it a much better hypothetical agent than citrate.

From the practical aspect it is important to note that the injection of Calcium Cevitamate is non-irritating and better tolerated than gluconate.

Summary

1. A comparative study of the solubility of Calcium Cevitamate and the gluconate shows the markedly greater solubility of the Calcium Cevitamate.

2. The yield of calcium ion per cc. of solution is from twenty to sixty times greater for Calcium Cevitamate than calglucon.

3. It is suggested that cevitamic acid participates with the parathyroid hormone in forming the diffusible ionized calcium of the serum calcium.

4. The field of calcium therapeusis is enlarged by the addition of a new soluble, non-irritating salt.

Spray Drying Produces Tiny Bubbles of Milk. *Science News Letter,* January 15, 1938. The new methods of spray drying which is used for milk, eggs, soap, potato flour or blood, were described at the Fourth Chemical Engineering Symposium held at the University of Pennsylvania.

If you have ever used any of these dried products you may have noticed that they may come in the form of tiny, dried bubbles which are light and hollow inside. It is spray drying which produces this unusual form. Additional solubility attained when one wants to put the dried product back into an edible or usable form is a merit of the method.

Ben B. Fogler and Robert V. Kleinschmidt of Arthur D. Little, Inc., described new techniques. It takes only from fifteen to thirty seconds for little liquid bubbles of the material to be dried into hollow spheres, they indicated. Great towers, sometimes two stories high, are employed. The sprayed solution comes in the top of the tower and drops by gravity during the drying. L. G.

EXPERIMENTAL PHARMACOLOGY AS A TEACHING TOOL*†

By Arno Viehoever**
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DEALING with the response of living units to drugs and medicines, pharmacology has a very definite and highly important objective. It must learn to understand life, and aspire to assist in the regulation of its mechanism, throughout its operation under all sorts of influences or conditions.

Thus pharmacology cannot help but be experimental. As it establishes the factors involved in the concrete relation between causes and effects, it places a yardstick of value on substances which may be found to be beneficial, harmful or inert to the living organism.

Pharmaceutical teaching will gain much by developing and using to its fullest extent a tool of such a dynamic force as experimental pharmacology may well be. As the teaching of experimental pharmacology, and particularly of the evaluation of drugs (bioassays), has been generally much neglected at medical schools, a great opportunity is before us in Pharmacy colleges.

In a recent discussion of Pharmacologic Research, Dr. Hans Molitor (see Merck Report) [1] enumerated these three principal divisions of applied pharmacology:

1. Therapeutic research, the investigation of better methods of the medicinal treatment of disease.

2. Research on Biologic standardization, the exact evaluation of the potency of drugs.

3. Toxicologic research, either in the field of preventive medicine or as forensic toxicology.

The U. S. P. Revision Committee, acknowledgedly has been a pioneer in introducing biological methods of evaluation as official bioassay methods. Leading U. S. manufacturers of biologicals and pharmaceuticals and Government laboratories have for decades employed workers in pharmacological control and research. The only com-

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†Reprinted from the *A. J. Pharm.*, Education 2, 46-50, 1938.
**From the Gross Laboratory for Biological and Biochemical Research.

prehensive survey of experimental pharmacology, as far as we know, is that of Heffter and Heubner.[2] In addition we have the stimulating books on pharmacological methods, e. g., by Burn,[3-4] Clark[5] or Sollmann and Hanzlik[6] and the extensive record of "Bioassays" by Munch[7] who recently published also a laboratory manual.[8]

While pharmacologic research has experimented in vitro, on isolated organs, on organ groups in situ, its most valuable work has or will be done on intact animals. Most impressive in its conclusiveness of results has been the biochemical vitamin work with controlled strains of rats, causing a food deficiency—by feeding diet lacking a specific vitamin—and then supplying it subsequently for recovery from the striking deficiency symptoms. Here the evidence of effects due to specific causes is fairly complete and so convincing that this type of experimental work has been introduced into classes where food chemistry, or biochemistry and biology are taught and even in the lower grades of public schools where the importance of adequate food is emphasized.

It is now generally admitted that all life, including the human, is subject to the same biological laws. The author and associates, most recently Dr. I. Cohen, have shown that no fundamental physiological differences exist between the invertebrates and vertebrates.[9-11] We thus may choose among the less complex animals those that respond alike with the organs and tissues of the three essential systems, muscular, glandular and nervous systems.

The author has selected a transparent crustacean, Daphnia magna, for a biological reagent.[10] Its standardization has given us a most welcome array of equal units for demonstration and research.

No typical substance, representative of physiologically active and thus pharmacological groups, has failed to produce specific effects and the scope, enumerated in the survey of Daphnia—the biological reagent, has been further widened.

Of *irritants,* the work on cantharidin[10] has been extended; it sulphonal have been tried in their depressing effects on organ functions and especially respiration and heart action. The preliminary results, already obtained with the assistance of Dr. Isadore Cohen, are gratifying.

Of *alkaloids,* the work on strychnine has been much extended in the recently published study of the mechanism of strychnine action

and the physiological evaluation.[11]* Brucine has been found to be much less toxic than strychnine, causing paralysis rather than convulsion. *Morphine,* as shown in preliminary experiments carried out with Mr. Robert Gilbert, causes rapid depression of organ function and especially the respiration and characteristic twitching of swimming organs, observable within three minutes in 1 per cent. solution of morphine sulphate.

Of *irritants,* the work on canthardin[10] has been extended; it has been shown that it is definitely unsuitable as a laxative as it is mainly locally active as a destructive agent. Elaterin was found to be a suitable substance, serving as a reference standard for organic laxatives.[12-13]

Vitamin E speeded up (several days) the release of eggs from the ovaries as embryos into the broodsac.

It is obvious that these results were but the outcome of extensive experimentation in breeding, application and recording. As a result, methods were worked out permitting quantitative and qualitative observations with a high degree of accuracy.

Thus a sound foundation is laid for the introduction of a laboratory course in experimental pharmacology. The costs for experimental animals and apparatus is so low that even departments without special budgets can undertake it.

The visibility of cause and effect through the transparency of organs is so obvious that a knowledge of their working mechanism is quickly acquired. The number of uniform standardized animals, steadily available, can be increased at will so that vigorous mature animals may be bred in any number needed, practically from week to week.

Those who have the funds, the staff, and the opportunity may want to expand their experiments to the use of the common vertebrate, but more complex laboratory animals. In one institution, which this author visited some years ago, animal experimentation was taboo due to the decision of the then acting Dean of Pharmacy.

While the author, (after more than ten years of experimentation), is convinced of the merit for the increased adoption of daphnia as an experimental animal, (see Cardinal Points in Favor of Daphnia),[14] experiments are continuously carried on in our Gross Re-

*A novel method, permitting wide application has been introduced, using the alternate depression and recovery of the normal heartbeat and respiratory rate as a means of comparing preparations of unknown strength.

search laboratory with vertebrate animals. This is done, mainly, for the purpose of checks of standardization as far as possible, and of tests suggested for bioassays and other phases of experimental pharmacology—as poisons and effective counteragents.

So many problems await solution, as potentiation of medicinal action; the replacement of habit-forming drugs as morphine; the discovery of efficient and specific antidotes for poisons; the isolation and preparation of the most efficient preparations and active substances; the most effective method of application; the judgment and control of drug value, etc.

It has been stated (1929, by Braun, Pharm. Ztg., N:1) that pharmacy had its eyes closed to pharmacology for the last fifty years. While this statement is obviously exaggerated we must now make every effort to see to it that, particularly, the younger generation of pharmacists appreciate the full importance of pharmacology and biochemistry, the least developed branches of physiology and chemistry. What better methods could we use than to supplement or to replace mere descriptive teaching with applied experimental pharmacology. We should use this applied science as a tool, opening with it the sealed mind of the students for the understanding of life, especially as influenced and benefited by drug action, or harmed by poisons.

With an orientation in the maze of life, and drug function as a guide, increased intelligent care can be given to the preparation, selection, and handling of worthy medicines on the part of the pharmacist. Medicine will hail this progress.

The workers capable of contributing to the safeguarding control of our drug supplies or to the actual advance of knowledge by carrying out research in experimental pharmacology, may be recruited, we trust, largely from students in Pharmacy.

It has been our happy experience that students, both undergraduate and graduate, can be readily inspired and encouraged by the results obtainable upon experiments with animals, (especially if transparent as Daphnia). We, therefore, urgently advocate experimental pharmacology as a valuable teaching tool and as a powerful weapon for medical and pharmaceutical progress.

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Research on Poliomyelitis Takes New Angle; Virus Strains Differ. *Science News Letter,* January 15, 1938. A new lead on the fight against infantile paralysis appears in research reported by Drs. James D. Trask and John R. Paul of Yale University School of Medicine.

Efforts to prevent the disease by nasal sprays of chemicals to block the nerve of smell have been based on the generally accepted belief that the virus which causes infantile paralysis enters the body through the nasal endings of the nerve of smell. The Yale investigators now have evidence which casts some doubt on all of this. Some strains of infantile paralysis virus will cause the disease in a large percentage of monkeys when simply injected under the skin, Drs. Trask and Paul found. These virus strains were recently isolated, some of them coming from patients in the Toronto epidemic last summer. Older virus strains, obtained long ago and kept growing in laboratories for years, rarely produce the disease unless injected into the nasal cavity. The difference between the strains may be only a coincidence, the Yale investigators point out. If it is not coincidence, it is obvious, although the scientists say nothing of this, that the fight against childhood plague will have to be approached from a somewhat different angle. L. G.

CHLORTHYMOL*

By Louis M. Roeg

CHLORTHYMOL became official in the National Formulary, 6th edition, on June 1, 1936. It has been used, however, since 1930 by various manufacturers of medicinal preparations.

Chlorthymol is a monochlorthymol. It is a white crystalline substance having an odor similar to thymol with an aromatic, very pungent taste. Its chemical formula is $C_6H_2.CH_3.OH.C_3H_7.Cl$ 1:3:4:6.

Chlorthymol is a powerful germicide, having fully 120 times the germicidal strength of phenol, when tested against Staphylococcus aureus, employing a resistant strain furnished by the Government. The germicidal properties of chlorthymol are not diminished by the presence of organic matter—in contrast to corrosive sublimate and the hypochlorites.

One gram of chlorthymol is soluble in 0.5 cc. of alcohol, but it requires 10,000 cc. of water to dissolve one gram. However, it will be explained that a mixture of alcohol, glycerin, and water enables one to obtain any desired concentration. Chlorthymol is used in antiseptic mouth washes. Methyl salicylate, oil of peppermint, and oil of spearmint are compatible with chlorthymol, but eucalyptol is not, as it forms with it an insoluble compound. A specially denaturated tax-free alcohol, namely No. 38-B may be used for chlorthymol. It contains 5 lbs. of methyl salicylate and 2½ lbs. each of oil of peppermint and oil of spearmint to 100 gallons of alcohol.

A special antiseptic mouth wash is recommended which has a concentration of 0.2 per cent. chlorthymol and contains 25 per cent. alcohol and 10 per cent. glycerin. Hence, 27 per cent. of specially denatured alcohol No. 38-B and 10.25 per cent. Glycerin U. S. P. are used as both have a strength of 95 per cent.

As chlorthymol is an effective germicide in the presence of various acids, there is also used in this antiseptic mouthwash 0.2 per cent. benzoic acid, 0.1 per cent. citric acid, 0.1 per cent. tartaric acid, and 5 per cent. boric acid.

After the entire mixture has aged for several days, it is to be filtered. Fuller's Earth is very suitable for obtaining a clear filtrate

*An address given before the local branch of the A. Ph. A. at Philadelphia, Dec. 14, 1937.

as the undesirable terpenes from the volatile oils are prevented by the Fuller's Earth from passing through the filter.

After filtration, this preparation may be colored by using various certified aniline colors, such as the newly certified Ponceau SX and certified Sunset Yellow.

The finished antiseptic mouth wash containing 0.2 per cent. chlorthymol is sufficiently potent so that before using one is to add four parts of water to one part of the antiseptic solution. The resulting dilution will then contain 0.04 per cent. chlorthymol and this concentration is germicidal against the resistant Staphylococcus Aureus, furnished by the Government.

It is also of interest that it is not necessary for the user to measure these quantities. A convenient amount of Antiseptic Chlorthymol mouth wash is placed in a glass and the water is then added; the first portion of the water produces a cloudy effect; but the mixture becomes clear upon adding the final portion—equalling the required four parts of water.

A hydro-alcoholic chlorthymol solution is also used as a germicide for cuts and abrasions.

By obtaining Specially Denatured Alcohol No. 38-B, containing 5 lbs. of Oil of Lavender flowers, and 5 lbs. of Methyl Salicylate per 100 gallons of alcohol, the preparation will have a clean, refreshing odor, suitable for a liquid to be applied to cuts and bruises. This germicide for cuts contains the same amount of chlorthymol, benzoic acid, citric acid, tartaric acid, boric acid, alcohol, glycerin, and water as is used in the previously described antiseptic mouth wash.

This antiseptic containing 0.2 per cent. chlorthymol may be diluted by mixing one gallon with four gallons of water, since the resulting dilution will although it contains only 0.04 per cent. chlorthymol be germicidal against Staphylococcus Aureus. The finished product is inexpensive as it contains only 2 per cent. glycerin and 5 per cent. of the tax-free Specially Denatured Alcohol No. 38-B. For making a sample batch, up to five gallons of the Specially Denatured Alcohol can be obtained from the various companies supplying alcohol without the basic permit. The preparation may be left water-white, or the desired shade imparted by using one of the certified colors already mentioned. Since a 0.04 per cent. chlorthymol solution is germicidal against Staphylococcus Aureus, the preparation

may be labelled with the term antiseptic or germicidal as part of the name of the product. The term disinfectant is applied to a product used for killing germs or inanimate objects—while a germicide, namely, an antiseptic which kills germs, is used for killing germs on man or beast and is a germicidal at body temperature.

As previously explained, chlorthymol and eucalyptol form a compound which is insoluble in water. It is only slightly soluble in a solution containing 26-29 per cent. alcohol, such as the antiseptic solution N. F. VI. The present formula specifies one gram of chlorthymol and 2 cc. of eucalyptol per 1000 cc., a large percentage of the chlorthymol and eucalyptol being removed during the filtration. To overcome this difficulty, members of the National Formulary Revision Committee have considered a modified antiseptic solution in which the thymol, chlorthymol, and menthol are to be reduced from one gram each to 0.5 gm. per 1000 cc. The eucalyptol is to be reduced from 2 cc. to 0.1 cc. per 1000 cc. The methyl salicylate and oil of thyme are to be reduced from 1.2 cc. and 0.3 cc. to 0.2 cc. and 0.01 cc. respectively per 1000 cc. This modified preparation is to be used undiluted. It has a pleasant taste and odor.

The strongest solution of chlorthymol possible in water is 0.01 per cent., namely, one gram per 10,000 cc. of water. This equals practically 1½ grains of chlorthymol to the quart of water. Such a solution will inhibit the growth of Staphylococcus Aureus. Hence, this aqueous solution would be called an antiseptic, providing its actual use permits a sufficient contact period to allow the inhibition of pathogenic bacteria.

A powder should therefore contain sufficient chlorthymol so that the quantity of the powder, to be added to a quart of water, will contain 1½ grains of chlorthymol.

Chlorthymol is chemically incompatible with alkaline substances, including soaps and calcium carbonate. In some cases, the chlorthymol is changed to thymol, thereby lowering its germicidal potency. In other cases, the ingredients in this group prevent the possibility of having an acid reaction which is an aid for the full germicidal effect of chlorthymol.

Chlorthymol is also used in ointments and oils, both mineral and fixed. At present, the Food and Drug Administration Methods of testing antiseptics are not applicable to all greasy substances because there is no suitable method which accomplishes proper contact

between an antiseptic chemical dissolved in a greasy substance and the micro-organisms in the aqueous culture media. This even applies to Phenol Ointment U. S. P. Hence, one cannot label such a preparation as being an antiseptic.

Chlorthymol is being used in Nasal Oil and in Baby Oil. The amount of the chlorthymol added is based on the quantity of phenol used in the Ointment of Phenol U. S. P. Thus 0.017 per cent. chlorthymol or 35 grains of chlorthymol to 30 pounds of the Nasal Oil or the Baby Oil, replaces 2 per cent. phenol; a quantity which would not be irritating. Chlorthymol is also used in ointments in the proportion of 105 grains of chlorthymol to 30 pounds of the ointment, namely, 0.05 per cent. chlorthymol replacing 6 per cent. phenol. This quantity would not be irritating. The chlorthymol is dissolved in twice its weight of an esential oil, such as volatile oil of camphor; then the solution of chlorthymol in the volatile oil is added to the mineral oil, vegetable oil or melted petrolatum when making respectively the Nasal Oil, Baby Oil or Ointment.

Vitaminizing of Margarine. Anon. *Amer. Jour. Public Health, 27,* 1226 (1937). Science's service to advance the welfare of the poor, as well as the rich, takes a new turn in the development of vitaminized margarine. According to a translation of a report from Denmark, the Danish Ministry of the Interior appointed a commission to consider the addition of vitamins to margarine. Several of the commission are distinguished physiologists. The group concluded that there was no doubt that vitaminizing of margarine with A and D vitamins will be of great importance in Denmark as many of the people will only in this manner be able to satisfy their natural vitamin requirements without exceeding their means.

It was recommended that all margarine should contain 14 to 18 International units of Vitamin A and 0.1 to 1.0 International unit of vitamin D per gram. The commission recommended that the vitamin A effect of margarine be secured by the addition of the vitamin itself along with carotene and in the same proportions as in butter. The recommendations were incorporated in an act of parliament and have already become effective. A. O.

CONSUMER RESEARCH, 1795 MODEL

By Mary North Chenoweth, Somers Point, N. J.

READERS of Professor LaWall's "Four Thousand Years of Pharmacy" may remember what he says concerning the quarrels between the English apothecaries and druggists of the 18th Century. A little known document in that controversy is "The History of Medicine" so far as it relates to the Profession of the Apothecary, from the earliest accounts to the present period: The Origin of Druggists, their gradual encroachments on Compound Pharmacy, and the evils to which the Public are from thence exposed; as also from the unskillful Practice of Ignorant Medicasters etc., Published at the Request of the Commitee of the General Pharmaceutic Association of Great Britain by John Mason Good, Fellow of the Medical Society of London, Member of the Corporation of Surgeons and author of the "Dissertation on the Diseases of Prisons and Poor-houses." London 1795. In this small octavo volume, Good traces to these conflicting interests, the inception of the General Pharmaceutic Association of Great Britain, which he thus describes: "It was to obtain redress against these evils (encroachment which the Chemists and druggists have of late years made on the profession of the apothecary . . . and the want of a competent jurisdiction in the profession itself . . .) and to restore to the profession a dignity and a purity which it ought ever to possess, that early in the spring of last year, several respectable apothecaries formed themselves into a society. They investigated these evils minutely, entered into an extensive correspondence with respectable members of their own profession, in almost every part of England and Wales, and endeavoured in every way to excite a spirit of universal enquiry and reformation. And having collected a volume of facts demonstrative of the infinite injury resulting to society at large as well as to the profession in particular from the toleration of these abuses, on the 17th of June 1794, a general meeting of the apothecaries of this kingdom was held at the Crown and Anchor, in the Strand, at which about two hundred practioners attended."

Our author addressed the gathering and in the latter half of his book he is reporting what he said at the Crown and Anchor "which he is enabled to give the more fully from short hand notes of a friend who did him the honor to write after him."

"If we regard personal views," he urged, "it was stated to be a fact, the proof of which was in the tables of calculation then present, that were the aggregate sums obtained by this infringement of the druggists, and divided amongst the druggists of this metropolis, a body of men unknown to the world till about the end of the last century, unauthorised by any public charter, and almost undescribed by any public act; were these sums to be equally divided, as they ought to be divided, amongst the apothecaries of this metropolis, every one would have an addition of nearly £200 a year to his present income. But this evil, it appeared, was not confined to the capital, though the apothecaries of London suffer more largely from its effects than their brethren in other situations. It was declared to be a morbific infection, that it began at the capital as at a central point, but diffused its deadly breath from thence to all the larger cities and towns throughout the Kingdom. Nor stopped the contagion here. From the larger cities and towns, it was beheld propagating itself to the smaller cities and towns, till at length, so general was the prevalence of the disease, there was scarcely to be found a village or a hamlet, without a village or a hamlet druggist. If the sale of medicines and the giving of advice was not here sufficient to support the vender, he added to his own occupation, the sale of mops, brooms, bacon, and butter, and a thousand such articles besides. The unanimity of country practitioners could not therefore be doubted of, in the adoption of any measures that might be devised to destroy this ruinous and ungenerous traffic of the druggist" . . .

"But it is not by personal views in a concern of such magnitude, we ought alone to be actuated . . . And, first, as to druggists: These, as well as all other warehousemen, engaged in the purchase of articles by the gross, must find those articles, when purchased, possest of different qualities. With respect to druggists it is so, in the purchase of rhubarb, Peruvian bark, gum Arabic, and, in effect, every foreign article besides. Hence an assortment becomes necessary. From this assortment the prime drugs only can be vended to the apothecary; for the apothecary is at all times, or at all times ought to be, a judge of their comparative quality. But what is to be done with the inferior assortments? To throw them away would be to destroy all profit accruing from the traffic with the apothecary; and to retain them, and not use them, would be precisely the same thing. And here the public, who can be no judge of the quality of

his materials, offers to the hesitating druggist a most ready, a most convenient, and a most welcome market indeed; and it is the only market that is offered to the druggist at all. But if, in the use of simple articles, he be exposed to such temptations, how may he hope to escape from the power of those stronger temptations which result from the preparation of compound medicaments and the extemporaneous prescriptions of physicians, in which succedaneums of inferior value are constantly soliciting his attention, and adulteration is never to be detected without severe labour and analysis. A druggist may, therefore, be a very honest man in the main, but he may have a large stock of indifferent materials on his hands and, in spite of his honesty, the temptation to dispose of these materials to the public will often be too strong to be resisted."

". . . Yet allowing the necessity of employing indifferent drugs in the composition of medical prescriptions, there is no necessity for compounding those prescriptions in a careless and unscientific manner and with wrong materials; or for sending wrong directions, or no directions at all with the prescriptions when compounded. But even these are facts which occur every day and the papers at this time on the table are sufficient, it was asserted, to substantiate the charge. They complain of some druggists who have made fatal mistakes in their compositions, of others who, from want of a classical education and an incapacity of translating the directions appended to their prescriptions have been under the necessity of disturbing apothecaries in the middle of the night to translate for them . . . There is rather a ludicrous mistake mentioned as having occurred in a druggist's house, in a letter from Croyden. The writer mentions his having been applied to by the foreman of this druggist for an explanation of the words 'cucurbita cruenta' which he had sought for in vain amongst the different preparations in his dispensatory; and at last, had been happy enough to translate them by 'an electric shock'? A druggist of similar penetration is reported in a letter from Worcester to exist in that city: this man is represented as taking infinite pains to obtain, through almost every druggist's shop, a tincture of the name of 'eiusdem' which, unluckily for the poor man, had been prescribed in a formula sent to his shop for preparation."

So far druggists; as to the drugs, the "Special Committee appointed to scrutinize the different specimens" procured "from more than a dozen of the most respectable druggists this metropolis will afford"—"specimens of a variety of drugs and preparations of the

present London Pharmacopœia, most material in the practice of Medicine, as also for the composition of a variety of extemporaneous prescriptions selected for this purpose"—reported as follows: "That in the far greater number of instances, there were most evidently spurious or defective drugs, and erroneous composition.

"That the different compositions of the same prescription were, in almost every instance, dissimilar from each other.

"That the most expensive medicines were all of them, without any exception, adulterated, as oil of cloves, oil of cinnamon, ladanum emplaster, cantharides emplaster, aromatic confection, sena-electuary, tinctures of guaiacum, cardamoms, rhubarb, etc., etc.

"That there scarcely appeared to be one instance of a medicine being faithfully prepared from the formula of the London Pharmacopœia; nor of a simple, but expensive drug, to be procured genuine. Such was the case, particularly with Aleppo scammony, with saffron, and Russian castor. Scammony could not be obtained pure even in its concrete state. The specimens of saffron were procured in the hay, as it is vulgarly called; and this form was determined upon, because least likely to be adulterated. But even of this there was no one specimen genuine; those which were sold having all of them an acrid taste, very foreign to what the saffron ought to possess and imparting little or no colour to spring water when infused in it. The Russian Castor was supplied by that from New England."

". . . So numerous, indeed and so important are these deceptions and abuses of the druggist that it is but a short time since a respectable apothecary of this city was under the necessity of returning to his druggist forty articles out of seventy-two that were sent him in consequence of their having been either not genuine, or improperly prepared. And it is not more than a fortnight from the time I am now writing, that a druggist of much respectability, told me of his having received a complete order to furnish another apothecary's shop at some little distance from him; but added that, as the gentleman who had sent the order, 'had desired him to be very particular in the selection of his articles,' he had himself, purchased more than half of them at the Apothecaries Hall! Here, therefore, is a druggist who has the ingenuousness to acknowledge that not half the medicines in his warehouse are genuine; and that, when he is obliged to send out medicines which are, genuine, he is under the necessity of applying to some other quarter for a supply."

The apothecaries, I submit, had a pretty case.

ABSTRACTS FROM AND REVIEWS OF THE LITERATURE OF THE SCIENCES SUPPORTING PUBLIC HEALTH

Bacteriology . . . . Louis Gershenfeld, B. Sc., Ph M.
Biochemistry, Nutrition, etc. . . . Arno Viehoever, Ph. D.
Biology . . . . . Marin S. Dunn, Ph. D.
Chemistry . . . . . Arthur Osol, Ph. D.
Pharmacy . . . . . E. Fullerton Cook, Ph. M.
and their assistants

The Value of Compound Tragacanth Powder as a Suspending Agent. J. M. Rowson. *Quart. Jour. Pharm. Pharmacol., 10,* 404 (1937). The addition of mucilage of acacia in any proportion to mucilage of tragacanth has been shown to result in a dehydration of the gel masses of tragacanth and their deposition as white floccules, the viscosity of the mixture being lower than that of either constituent mucilage. A minimum viscosity was attained in a mixture consisting of 80 per cent. of mucilage of tragacanth and 20 per cent. of mucilage of acacia. Similar results were obtained when these mixtures were diluted with seven volumes of water and the viscosities and suspending powers measured; although a minimum value was found at a different concentration.

The presence of the relatively small quantity of acacia in compound tragacanth powder has been shown to produce a considerable reduction in the viscosity and suspending power of the tragacanth constituent either in the presence or absence of electrolytes in solution. No similar reduction is brought about by the starch or sucrose present, and it is suggested that the acacia be omitted from this preparation, the starch and sucrose being retained to insure smooth dispersion of the tragacanth when mixed with water. A. O.

Determination of Zinc Oxide in Ointment. W. Awe. *Pharm. Zentralh. 77,* 589 (1936) through *Quart. J. Pharm. & Pharmacol. 10,* 555 (1937). A sample of the ointment of about 2.5 Gm. accurately weighed is shaken in a glass-stoppered flask with 30 cc. $CHCl_3$ or CCl_4 and 50 cc. n/2 HCl until a clear solution is obtained. The

whole is transferred to a separator, the $CHCl_3$ layer separated and the aqueous layer washed twice with 10 cc. of $CHCl_3$ which is added to the $CHCl_3$ extract. The combined $CHCl_3$ extracts are washed with 25 cc. of water which is added to the aqueous extract which is then made up to 250 cc. by the addition of water. A 100 cc. portion of this aqueous solution is next titrated with alkali using methyl orange indicator until the color is the same as that given by 1 drop of n/10 hydrochloric acid in 100 cc. of water plus the indicator. Evaporation of the $CHCl_3$ extract gives the amount of base in the ointment, should this be desired. L. F. T.

The Effect of Certain Substances on the Absorption of Insulin. E. M. Bavin and W. A. Broom. *Quart. J. Pharm & Pharmacol. 10,* 325 (1937).

Part I—Metals.

The authors report on the effect of various metals including zinc, magnesium, and iron in different concentrations on the hypoglycemic action of insulin. Zinc up to 25 mg. per 500 units had no effect on the insulin response, 75 mg. caused a very slight prolongation, 200 mg. produced a definite delay in the return to the normal fasting level. Above these amounts the inhibitory effect became increasingly apparent until at a concentration of 2750 mg. of zinc per 500 units the hypoglycemic action was completely inhibited for 13 hours. Magnesium prolonged the hypoglycemic action at a concentration of 1500 mg./500 units, inhibition occurred at 12,500 mg./500 and complete inhibition at 25,000 mg./500 units. Iron behaved in a similar manner in concentrations ranging somewhat lower than those of magnesium but higher than those of zinc.

Since no hyperglycemic action was observed from the metals *per se* two possible mechanisms are suggested. The metal may attach itself to the active groups of the insulin molecule and thus render it incapable of producing its normal response or, secondly, the metals in the rather large concentrations may exert a toxic effect on some stage of carbohydrate metabolism. The necessity for the presence of zinc in the formation of crystalline insulin and its effect in increasing the action of protamine lends support to the hypothesis that zinc can combine with the insulin molecule. In such a case, however, it would be expected that the smaller the atomic weight of the metal used the smaller would be the concentration necessary to produce

inhibition. This is not borne out, however, by the above results wherein more magnesium is required than zinc.

Part II—Tannic Acid and Zinc.

The combination of tannic acid with insulin has been shown previously by Bischoff and Maxwell (*J. Biol. Chem. 114,* 11 (1936)) to have a more prolonged hypoglycemic action than insulin alone. Hagedorn (*Proc. Roy. Soc. Med. 30,* 805 (1937)) discarded the combination clinically because of local reactions. Scott & Fisher (*J. Pharmacol. 58,* 78 (1936)) demonstrated that zinc had a similar action on the insulin tannate as upon the protamine-insulin complex.

Investigations were carried out for the purpose of determining if the local reactions due to the tannin could be avoided and also to determine the lowest proportion of tannic acid to insulin which would produce a maximum delay in hypoglycemic response.

Employing a combination of tannic acid and insulin 2:1 and zinc in the ratio of 1 mg. 1 unit blood sugar curves were obtained paralleling those obtained with protamine-zinc insulin. The ratio of 2:1 for tannic acid-insulin was the lowest which produced maximum delay in hypoglycemic response and in this ratio the insulin was found to be 99-100 per cent. precipitated.

The unfavorable results obtained by other workers through local irritation following injection is thought to be due to the excessive tannic acid ratio employed. Clinical trial of this new combination appears justifiable. L. F. T.

The Absorption of Drugs and Poisons Through the Skin and Mucous Membranes. D. I. Macht. *J. A. M. A. 110* (1938). The author briefly reviews his many contributions relative to the absorption of drugs published during the past twenty or more years; researches demonstrating such now well accepted facts as the ready absorption of many drugs through the mucous membranes of the nose, urethra, vagina, etc.

In this paper is presented the results of several years' studies on the absorption of drugs through normal skin and mucosa as well as through pathologic tissue. The use of fixed oils and fats as vehicles in order to carry drugs into the deeper layers of the skin provided very inefficient penetration whereas the volatile oils are readily absorbed through the skin producing profound physiologic and pathologic effects often ending in death. Some of these volatile

oils were employed as vehicles for more powerful drugs whose absorption they greatly promoted.

Studies of a series of pure chemical constituents of the volatile or essential oils revealed that most of them were easily absorbed both through the skin and mucous membranes. Many of these were quite poisonous but when diluted with alcohol and other solvents they may be utilized as vehicles for carrying other active drugs into deeper layers of the skin. It was clearly demonstrated experimentally that the penetration of the skin of mice and rats by morphine, strychnine, atropine, pilocarpine and other drugs can be facilitated by incorporating them in such vehicles. This knowledge is of obvious importance from the standpoint of applied therapeutics since it offers a rational basis for various time-honored therapeutic procedures employed by the best of the older physicians. It was shown, for instance, that the use of phenol in glycerin for infection of the middle ear has a rational basis. It has also been demonstrated by these experiments that the efficiency of turpentine stupes applied to the abdomen for the relief of gas pains is actually due to the absorption of the terpenes through the skin. The use of opium lotions for injuries to the eye has a rational pharmacologic basis. Studies on pathologic mucous membranes and skin were found to speak for the efficacy of astringents in the treatment of diseases of the throat and experimentally support the modern treatment of burns with tannic acid and silver nitrate. L. F. T.

Effect of Benzedrine Sulfate on the Emptying Time of the Human Stomach. E. J. Van Liere and C. K. Sleeth. *J. Pharm. & Exper. Therap. 62,* 111 (1938). Despite the fact that benzedrine sulfate is a relatively new drug, several important therapeutic uses have already been found for it. Of considerable interest is a report by Myerson and Ritvo (*J. A. M. A. 107,* 24 (1936)) who advocated its use in roentgen study of the gastro-enteric tract and reported that it allayed gastro-intestinal spasm so that it could be employed not only to control certain spastic conditions but also to differentiate between functional and organic spasm.

The authors studied the effect of benzedrine sulfate on the stomach emptying time, reasoning that if it did allay gastro-intestinal spasm it should function in prolonging this function also. It was clearly demonstrated to markedly delay gastric emptying time in a manner

similar to that produced by ephedrine. Myerson and Ritvo *ibid.* reported the stomach to empty faster under the influence of benzedrine with the explanation that it relaxed the pyloric sphincter and thus allowed the material in the stomach to pass out more quickly. This observation may have arisen from a study of the type of gastric peristalsis which is not believed to be as good a criterion as the amount of chyme extruded over a period of time, which is easily determined by ascertaining the time required for the stomach to empty.

Since benzedrine sulfate stimulates the sympathetic fibers it is reasonable to suppose that the peristalses of the small intestines are also lessened; thus if the drug were used continuously a certain amount of intestinal stasis might ensue. Whether this depression would be sufficient to produce disagreeable symptoms such as constipation, flatulence, etc., needs further study. L. F. T.

Mysterious Epidemic Cause of Recent Infant Illness. *Science News Letter,* January 15, 1938. The mysterious diarrheal malady that has afflicted infants in Chicago hospitals is not limited to that city. Epidemics of the same sort and probably the same disease have occurred in many cities in this country and abroad, according to a report by Drs. Samuel Frant and Harold Abramson of The New York City Health Department (*American Journal of Public Health,* January).

The malady has been responsible for a steady increase in mortality among the new-born babies in recent years, they declare. This increase in babies' deaths is to be found chiefly among infants one month old or less.

The malady is epidemic diarrhea of the new-born. It is not related to the summer diarrhea which took such frightful toll of babies a generation ago. This new malady afflicts infants born in hospitals, and strikes during the first three or four weeks of life. No cause has yet been found for the disease. It has been reported in Seattle, Toronto, Memphis, New York, Chicago, Rochester, N. Y., Buffalo, Teaneck, N. J., Cincinnati, Cleveland, Edinburgh, Scotland, and Garches, France. In New York in the past three years, 23 such outbreaks have occurred, affecting 711 infants of whom 335 died.

The only known way of fighting the disease at present is to break the chain of infection from one infant to another in hospital nurseries.

Usual methods of safeguarding infants in hospital nurseries have apparently not been sufficient to prevent the spread of this disease once it starts, and consequently Drs. Frant and Abramson recommend certain new methods to doctors and hospital authorities.

L. G.

Powerful Microscope Makes Very Tiny Objects Visible. *Science News Letter,* January 15, 1938. New inroads into the world of the small are envisioned now as a result of construction at Harvard University of a miscroscope more than four times as powerful as any microscope ever built before. Designed by two Harvard geologists, Drs. E. C. Dane, Jr., and L. C. Graton, Harvard's new instrument can magnify up to 50,000 diameters. Its effective magnification—the limit at which no new details are shown—is 6,000 diameters, more than four times the previous limit. So powerful is it in comparison to its smaller contemporaries that it far surpasses what was believed by scientists a year ago to be the theoretical limit of the usefulness of a miscroscope. Much of this magnification is "empty," resembling that of a large photographic print produced from a miniature negative. Effective magnification, producing more visible detail as it increases, up to 6,000 diameters, is secured with this instrument. Weighing about a ton, this microscope is mounted on the steel bed of a lathe, to secure stability. So fine are the focussing screws that it would take twenty-five minutes of rapidly turning them by hand to produce a motion of 1/400 of an inch. Motors, with several speeds, do the turning more quickly.

Used chiefly for examining ores, this microscope catches images too small to be detected by ordinary instruments. Objects only 100 times as large as an atom can be seen and photographed. With the theoretical limits already passed, there seems to be no reason why even greater magnifications, with lenses designed according to revised theories cannot be made. Already, another of these microscopes, patterned after the original model, but slightly improved, has been installed by the Canadian Department of Mines, in Ottawa, to be used in the minute study of ore. L. G.

Migraine Headache Called Perpetual Emotional Drunk. *Science News Letter,* January 15, 1938. A person with migraine headache is on a perpetual emotional drunk, Dr. Milton B. Jensen,

consulting psychologist of Louisville, Ky., reported to the recent meeting of the American Association for the Advancement of Science at Indianapolis.

Simple habits of becoming extremely excited over everything or nothing were blamed by Dr. Jensen with this puzzling and painful type of headache without organic cause. In his (or her) emotional sprees, the individual tenses his muscles so that he produces a partial anemia in the brain by reducing the circulation of the blood. The headache results from a stretching of the blood vessels in the brain.

Sex cannot be blamed for migraine, Dr. Jensen declared:

"Sexual maladjustment bears no causal relationship to the onset, duration, frequency, or severity of ordinary migraine headaches," he said. "Maladjustment to sex does not cause the headache and the headaches do not cause sexual maladjustment."

Too much excitement in the home during childhood, improper rest and acquired habits of incessant nervous excitation were held responsible. Dr. Jensen cited cases where the headaches cleared up when the sufferers learned to control their emotional responses.

L. G.

Nasal Spraying Seems Best Hope of Preventing Poliomyelitis. *Science News Letter,* January 15, 1938. New research which gives a clue to the mechanism that gives the immunity to infantile paralysis and seems to show that spraying of the nose with chemical or other germ-fighting agents will eventually prove the means of preventing this crippling malady was reported at the meetings of the Society of American Bacteriologists. In actual practice with children, the method has so far not been anything like 100 per cent. successful. But from reports presented, it appears that the method is fundamentally sound and that success is only a matter of perfecting details, such as finding the best substance to spray and the surest way of getting the spray onto the strategic area. The lining of the nose appears to be the key to the situation. Not only does the virus of the disease enter the body through this lining, but resistance to the virus develops naturally in this lining. This last important point appears from research reported by Drs. Albert B. Sabin and Peter K. Olitsky of the Rockefeller Institute for Medical Research. They found that when a monkey becomes immune to the disease, as a result of having had one attack, the cells of the membranes that line his nose

contain anti-bodies that can dispose of the infantile paralysis virus and prevent its getting at the nerves to destory them and cause paralysis of muscles. Nasal sprays have been used heretofore with the idea that they could block the passage of the virus by sealing up the membranes. Drs. Sabin and Olitsky investigated this point also, but so far have been unable to discover whether this actually is the case or whether the chemical of the spray exerts its protective action in some other way. Of all the chemicals they tested, zinc sulfate was the most effective for protecting monkeys against the disease.

Dr. E. W. Schultz, of Stanford University, pointed out that loss of the sense of smell after the nose has been sprayed with zinc sulfate is a sign that the spraying has been done thoroughly enough to protect the child or adult against infantile paralysis.

Dr. Schultz is leader of one of the research teams that found zinc sulfate nasal sprays effective in protecting monkeys against the disease. Reason for the failure of the spray to give children as much protection as it does monkeys is because the spraying was not done thoroughly enough, Dr. Schultz believes. The virus which causes infantile paralysis gets into the body through the tiny hair-like endings of the nerve of smell. When these nerve endings are destroyed by chemicals, the virus apparent cannot get through. Destruction of the nerve endings can be detected by testing the sense of smell. When it is lost—scientists call the condition anosmia—Dr. Schultz believes it is a sign that the child is protected against the disease. The loss is only temporary, as the nerve endings regenerate. In children the loss of sense of smell following chemical spraying may last only three or four days, and in adults it may be lost for a few months. When the sense of small returns, it is time to spray again, if infantile paralysis is still prevalent in the neighborhood.

Vaccination will not protect against infantile paralysis because vaccination is only effective against germs that get into the blood. The infantile paralysis virus which travels nerve routes rather than the blood route must be fought by chemicals that will strengthen nerve resistance. So far, no way of doing this other than by chemical blockade of the nerve endings with a spray is known. L. G.

Sulphanilamide and Virus Diseases. E. B. McKinley, E. G. Acree and J. S. Meck. *Science,* No. 87, No. 2246, 43, 1938. Since the report of Domagk in 1935 concerning the chemotherapeutic action

of Prontosil in streptococcal infections, it has been found that a fraction of the Prontosil molecule, para-aminobenzene sulphonamide (sulphanilamide) is also effective in streptococcal infections and in a few other bacterial infections as well (meningitis, gonorrhea, etc.).

Naturally one of the early questions which arose was the possibility of using these chemotherapeutic agents in virus diseases. In September, 1937, Rosenthal, Wooley and Bauer reported that Prontosil possessed therapeutic activity against the virus of choriomeningitis in mice but that sulphanilamide and Prontosil Soluble were inactive.

The above authors have recently tested experimentally three additional virus diseases with sulphanilamide (Prontylin) with results similar to those described by other workers. Since this subject is a very active one in the field of medical research at the present moment and since the mode of action of these drugs is of such interest, attention is directed to the apparent negative action of sulphanilamide on the virus diseases tested.

Employing sufficient numbers of animals for experimental infection and for controls the activity of sulphanilamide against the viruses of poliomyelitis, rabbit fibroma and rabbit myxomatosis was tested. In the poliomyelitis experiments a group of monkeys was inoculated intracerebrally with mixed poliomyelitis virus. Forty-eight hours later several of these animals were given subcutaneous injections of sulphanilamide, while others received no treatment with the drug and were kept as controls. The animals treated were given one-half gram of the drug, suspended in physiological salt solution, per kilogram of body weight. The treatments were continued for five successive days. The animals received a total of from six to twelve grams of the drug, depending upon their weights. All the monkeys died, including the controls, in from ten to fourteen days with typical symptoms of poliomyelitis except one monkey, which survived for twenty-seven days. This animal had received the drug daily for five days, beginning forty-eight hours following the injection, and a total of 9.1 grams of sulphanilamide were administered. Kelson has also reported negative results in experimental poliomyelitis when animals were infected by the intranasal route.

Rabbits experimentally infected with fibroma and myxoma viruses, respectively, were also given subcutaneous treatments with the drug. The dosage used was the same as in the experiments with

poliomyelitis virus. An equal number of infected, but untreated animals were kept for controls. In the case of myxoma virus, all the animals, both treated and untreated, died with myxomatosis on the tenth to twelfth day following injection with the virus. Treatments with sulphanilamide were begun forty-eight hours following injection with virus and were continued for three successive days. Experiments with fibroma virus were carried out similarly, and all animals, treated and untreated, developed fibroma, except for two controls which died of an intercurrent infection.

These negative results with sulphanilamide in treating experimental virus infections raise certain questions regarding the mode of action of this drug, particularly in view of a few bacterial diseases in which it is apparently highly efficacious. One of the essential differences between virus and bacterial infections is that the former are invariably of an *intracellular* nature while the latter are chiefly *intercellular,* though in some bacterial diseases cellular invasion is also characteristic. It is suggested that sulphanilamide is unable to exert its action (?-bacteriostatic, virustatic or what-not) against the infecting agent when it has invaded the tissue cells as in the case of virus infections. The efficacy of sulphanilamide in specific bacterial diseases may depend partly on its successful attack against extracellular organisms, while the host cells themselves are contributing to the defense against the invading microbes. On the other hand, we may assume from present evidence that viruses find conditions within the tissue cells favorable, rather than unfavorable, for survival and multiplications. L. G.

Tuberculosis, Leprosy and Alied Mycobacterial Diseases. E. R. Long, *Science,* 87, No. 2246, 23, 1938. Dr. Long in his address as vice-president and chairman of the section on the Medical Sciences, American Association for the Advancement of Science, at the Indianapolis meeting in December, 1937, presented interesting and valuable data concerning the above diseases, a summary of which follows:

1. Tuberculosis, leprosy and the "skin lesion" disease of cattle, Johne's disease, rat "leprosy" and a series of ill-defined ailments of rodents, cold-blooded animals and birds, constitute a group of diseases of spontaneous natural occurrence, with two distinctive features in common: (1) causation by mycobacteria, i. e., bacteria dis-

tinguished by the staining property of acid-fastness, due in turn apparently to mutual possession of certain chemical substances, and (2) a host response characterized by extensive proliferation and accumulation of large mononuclear phagocytes, or monocytes, and their development into "epithelioid" cells.

2. In addition to the naturally occurring mycobacterial diseases, just listed, a wide variety of disease processes caused by acid-fast bacteria can be induced experimentally by infecting different animals with the various bacilli of the group. Variations as follows can be produced at will:

(a) From one strain of mycobacteria in different animal species.
(b) From different strains of mycobacteria in one animal species.
(c) From one strain of mycobacteria in one animal species modified by immunization.
(d) From one strain of mycobacteria in one animal species with genetic variability in susceptibility.
(e) From the dissociated elements of one strain of mycobacteria in one animal species.

Thus a wide variety of mycobacterial diseases occurs as a result of animal and bacterial variability.

3. Although host and infecting agent are variables, constants occur in the chemical constituents of the two. Of the chemistry of the cells of the animal body which accumulate in the characteristic lesion of this group of diseases, little significance is known. In contrast much information is available on the chemistry of artificially grown mycobacteria. Lipids, proteins and carbohydrates are distinctive, qualitative and quantitative differences being detectable within the group. The lipids act as stimulants for the large mononuclear phagocytic cells, and the proteins also call them forth in the acute processes of the diseases concerned. In general the inflammatory exudations and the toxic necroses seem to be the result of protein action, particularly after "hypersensitiveness" is induced in the course of the disease, while the chronic changes are due in large measure to the bacillary lipids. The ultimate "epithelioid" appearance of the characteristic cells making up the lesions of the several diseases concerned appears to be the result of destruction of acid-

fast bacilli within them and cytoplasmal dispersion of their constituent lipids. Some of the carbohydrates as well as proteins appear to be toxic for animal cells.

4. With these facts at hand the great variability of mycobacterial disease is understandable as the result of interplay of variable bacteria and variable animal cells, each with its individually characteristic content of biologically active chemical constituents. This can be shown readily for the experimental disease in the laboratory, and the facts brought to light suggest plausible explanations for the great variability of spontaneous mycobacterial disease in nature. L. G.

Thermal Microscope Shows Crystal Formation at 3632° F. *Science News Letter,* January 15, 1938. Search for synthetic abrasives rivalling the diamond in hardness has led to the development of a new "thermal microscope" which makes possible the observation of crystal formation and change even at high temperatures of as much as 3,632 degrees Fahrenheit. This new tool of science was disclosed in an address by Dr. Frank J. Tone, president of the Carborundum Company, Niagara Falls, N. Y., as he accepted the prized Perkin Medal for 1938. The Perkin Medal is awarded annually by the American Section of the Society of Chemical Industry, an international chemical organization. The diamond, said Dr. Tone, still stands as the peer of all abrasives despite various reports from time to time that some synthetic material is "just as hard." Silicon carbide—familiar carborundum—and fused alumina are the next ranking abrasive materials, said Dr. Tone, which are available and widely used in commercial quantities. But there are other new abrasives which appear to be superior to silicon carbide. Boron carbide is one which can be bonded with silicon carbide to form a superior cutting stone. A basic handicap to the development of the very hard cutting materials has been the inability of scientists to study their structure effectively. The new thermal microscope, which Dr. Tone described, is one new tool which make possible more knowledge about these hardest of synthetic man-made materials. Motion picture attachments are now used with the thermal microscope so that a continuous, permanent record can be made of the formation of such material as crystalline silicon carbide at temperatures over 3,632 degrees Fahrenheit, or 2,000 degrees Centigrade. L. G.

BOOK REVIEWS

Done by persons, unafraid to upbraid, but perfectly willing to give praise where praise is really due.

GENETICS AND THE ORIGIN OF SPECIES. Theodosius Dobzhansky, Columbia University Press. 363 pages, 1937.

To those who have not kept pace with the recent developments of genetics and cytology but who are still interested in problems of evolution, this book has to offer a veritable world of information and a new approach in the understanding of evolutionary processes. It should be thoroughly understood that a solution to the mystery of the origin of species is not advanced. Instead, there is found a summary and synthesis of the new experimental evidence of genetics which no evolutionary theory can ignore in dealing with the problem of mechanisms of evolution.

Genetics and the Origin of Species is based on a series of lectures delivered at Columbia University in 1936. The material presented does not lend itself to casual reading but demands study, digestion and assimilation—thus can its full value be appreciated.

There are ten chapters which deal with the following subjects and their ramifications: organic diversity, gene mutation, mutation as a basis for racial and specific differences, chromosomal changes, variation in natural populations, selection, polyploidy, isolating mechanisms, hybrid sterility and, finally, species as natural units. A general idea of the author's thesis might be reached by quoting here a few of the salient points.

"To a geneticist organic diversity is one of the most fundamental properties of living matter; diversity is here considered so to speak, as an aspect of unity through a study of mechanisms which may be responsible for the production and maintenance of variation, an analysis of the conflicting forces tending to increase or level off the differences between organisms.

"Since evolution is a change in the genetic composition of populations, the mechanisms of evolution constitute problems of population genetics. The mechanisms of evolution as seen by the geneticist appear as follows. Gene changes, mutations, are the most obvious source of evolutionary changes and of diversity in general. Next come the changes of a grosser mechanical kind involving rearrange-

ments of genic materials within the chromosomes. Finally, reduplications and losses of whole chromosome sets (polyploidy) are important as evolutionary forces, especially among some plants. Mutations and chromosomal changes arise in every sufficiently studied organism with a certain finite frequency, thus constantly and unremittingly supply the raw material for evolution. The influences of selection, migration, and geographical isolation then mold the genetic structure of new populations with new shapes, in conformity with the secular environment and the ecology, especially in the breeding habits, of the species. This is the second level of evolutionary process, on which the impact of the environment produces historical changes in the living population. Finally, the third level is a realm of fixation of diversity already attained on the preceding two levels. Races and species as discrete array of individuals may exist only so long as the genetic structures of their populations are preserved distinct by some mechanisms which prevent their interbreeding."

It may be well to reiterate that this book does not concern itself with the usual semi-popular treatment of evolution that one generally encounters upon the library shelf. Such treatment is merely a consideration of the static factors and can contribute little towards revealing the mechanisms of dynamic evolutionary processes. While such treatment has an aesthetic appeal, the author believes that the "rapidly growing body of both observational and purely experimental evidence gives at least a promise that an adequate analysis of evolutionary dynamics will be possible in a not too distant future."

Isadore Cohen.

PILLSBURY, ARTHUR C. PICTURING MIRACLES OF PLANT AND ANIMAL LIFE. 236 pp. 66 illustrations. J. B. Lippincott Co., Philadelphia, 1937.

Anyone who is at all interested in natural science or in photography should read this work, describing, as it does, simply and clearly, the author's gradual development of the lapse-time method. It is unusual, refreshing and stimulating, recording not only methods but also careful observations concerning subject matter made by a man who has strikingly pioneered in his search for truth. With his love of living things and with his desire to learn the truth about how they live and work, the author has the advantage of a background of me-

chanical engineering. He has applied this training to the assemblage and use of his photographic equipment.

The volume deals, among other things, with the lapse-time method for the reactions of flowers (Snow Plant, Western Blue Flag Iris, Blazing Star, Stream Orchid, Mariposa Tulip, Evening Primrose, Dandelion, California Poppy, etc.), pollenization (milkweed, Monk's Hood Orchid, etc.), microscopic motion photography (including the observations made on the living nucleus of the Spider Lily), experiences in photographing cacti, the story of the bread mold, x-ray motion pictures (shadowgraphs of the opening of a rosebud are shown), undersea photography (methods and dangers), the traveling camera, technicolor, and the use of polarized light. A chapter is devoted to some of the author's experiences in chemical farming. A formula for a simplified general culture solution is given together with directions for use.

Marin S. Dunn.

Hope of Preventing Fatal Blood Clots Renewed. *Science News Letter,* January 22, 1938. Renewed hope of preventing fatal blood clots after surgical operations appears in the report of Drs. D. W. G. Murray, and C. H. Best of the University of Toronto Faculty of Medicine. Heparin, an anti-blood clotting substance from the liver, has been prepared in such pure form that it can be safely given to humans without danger of poisoning, the Toronto investigators report. It prevents the development of blood clots (thrombosis) in the veins of dogs. In their report the Toronto investigators state that this purified heparin has now been given to 220 patients after operation at the University Hospital and also to a group of patients in Sweden. It was pointed out that many times this number of patients must be studied before any conclusions as to the effectiveness of heparin in preventing thrombosis can be reached. Heparin and its anti-bloodclotting property were first discovered by Dr. William H. Howell of Johns Hopkins University. L. G.